

WHAT IS CLAIMED IS:

1. A method for identifying a compound that modulates the level of a lipid or lipoprotein in a nematode comprising :

5 (a) contacting a compound with test nematodes;

 (b) comparing a phenotype of said test nematodes with said phenotype of nematodes not contacted with said compound, wherein a modification of said phenotype correlates with a modulated level of a lipid or lipoprotein, said phenotype being selected from the group consisting of (i) length of defecation cycle; (ii) rate of germline development relative to rate of soma development; (iii) rate of embryonic development; and (iv) rate of post-embryonic development,

10 whereby a difference in said phenotypes identifies said compound.

2. A method for isolating a gene that modulates the level of a lipid or lipoprotein in nematodes comprising:

15 (a) subjecting nematodes that comprise at least one mutation in the clk-1 gene to mutagenesis to produce test nematodes;

 (b) identifying test nematodes that exhibit a phenotype that is modified as compared to the phenotype of nematodes not subjected to mutagenesis, wherein said phenotype that is modified indicates a modulated level of a lipid or lipoprotein, said phenotype being selected from the group consisting of (i) length of defecation cycle; (ii) rate of germline development relative to rate of soma development; (iii) rate of embryonic development; and (iv) rate of post-embryonic development; and

20 (c) cloning the gene that was mutated in step (a) from a test nematode of step (b).

25 3. A method for identifying a gene that modulates the level of a lipid or lipoprotein in nematodes comprising (a) contacting test nematodes that comprise at least one mutation in the clk-1 gene with a nucleic acid that reduces specifically the level of expression of a nematode gene; and (b) identifying test nematodes that exhibit a phenotype that is modified as compared to the phenotype of nematodes not contacted with said nucleic acid, wherein a modification of said phenotype in said test nematodes indicates that the nematode gene in said test nematodes modulates the level of a lipid or lipoprotein, said phenotype being selected from the group consisting of (i) length of defecation cycle; (ii) rate of germline

development relative to rate of soma development; (iii) rate of embryonic development; and (iv) rate of post-embryonic development.

4. The method of claim 3, wherein the nucleic acid is selected from the group

5 consisting of an antisense nucleic acid, and a double-stranded RNA molecule.

5. The method of claim 4, wherein said contacting comprises feeding nematode with bacteria comprising said nucleic acid.

10 6. A method for selecting nematodes having modulated level of a lipid or lipoprotein comprising:

(a) treating test nematodes to modulate the level of a lipid or lipoprotein; and

(b) identifying test nematodes that exhibit a phenotype that is modified as compared to the phenotype of nematodes that has not been treated, wherein a modulated level of a lipid 15 or lipoprotein in said test nematodes is indicated by the phenotype that is modified, said phenotype selected from the group consisting of (i) length of defecation cycle; (ii) rate of germline development relative to rate of soma development; (iii) rate of embryonic development; and (iv) rate of post-embryonic development.

20 7. The method of claim 1 or 6, wherein the test nematodes comprise (a) at least one mutation in the clk-1 gene; (b) at least one mutation in the clk-1 gene and at least one mutation in the dsc-3 gene; or (c) at least one mutation in the clk-1 gene and at least one mutation in the dsc-4 gene.

25 8. The method of claim 1, 2, 3, 4, 5, or 6, wherein the phenotype of said test nematodes in step (b) is modified by (i) a decreased length of defecation cycle; (ii) an increased rate of germline development relative to rate of soma development; (iii) an increased rate of embryonic development; or (iv) an increased rate of post-embryonic development.

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9. An isolated nucleic acid comprising:

(a) the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:7;

(b) a nucleotide sequence that encodes the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:8

(c) a nucleotide sequence that is at least 80% identical to the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:7;

(d) a nucleotide sequence that is a complement of (a), (b) or (c),
with the proviso that the nucleic acid does not comprise genomic sequences that are

5 contiguous to SEQ ID NO: 1 or 7, or that are contiguous to a subsequence of SEQ ID NO: 1 or 7.

10. An isolated nucleic acid that hybridizes under stringent conditions to:

(a) a nucleic acid probe that consists of the nucleotide sequence of SEQ ID NO:1 or

10 SEQ ID NO:7; or

(b) a complement of (a);

with the proviso that the isolated nucleic acid is not the nucleic acid of one of the clones designated yk357a6, K02D7, H06H21, or Y17G9.

15 11. The nucleic acid of claim 10, wherein the nucleic acid is a double-stranded RNA molecule.

20 12. The nucleic acid of claim 10 wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO:1 except that the nucleotide residue at nucleotide 354 is a thymine residue and the nucleotide at position 605 is an adenine residue.

25 13. The nucleic acid of claim 10 wherein the nucleic acid comprises a nucleotide sequence that encodes a polypeptide consisting of a fragment of the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:8, wherein said polypeptide displays one or more functional activities of the DSC-3 or DSC-4 polypeptide.

14. An isolated polypeptide comprising SEQ ID NO:2 or SEQ ID NO:8.

30 15. A fragment of a polypeptide comprising at least 8 consecutive amino acids of the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:8.

16. A polypeptide comprising an amino acid sequence that has at least 60% identity to the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:8.

17. The polypeptide of claim 14 wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:2 except that the amino acid residue at position 62 is a phenylalanine residue and the amino acid residue at position 146 is a threonine residue.

5 18. An antibody that immunospecifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:8, or a fragment thereof.

19. An expression vector comprising the nucleic acid of claim 9.

10 20. A cell comprising a recombinant nucleic acid comprising the nucleic acid of claim 9.

21. A transgenic non-human animal comprising a transgene that comprises the nucleic acid of claim 9 or 10.

15 22. The transgenic non-human animal of claim 21, which is a *C. elegans* nematode.

23. A method for making a polypeptide comprising the steps of:

20 (a) culturing a cell comprising a recombinant MOLL nucleic acid under conditions that allow a MOLL polypeptide to be expressed by said cell; and
(b) isolating the MOLL polypeptide.

24. A method for identifying a compound that binds a MOLL polypeptide comprising the steps of:

25 (a) contacting a MOLL polypeptide with a test compound under conditions that allow said test compound to bind said MOLL polypeptide; and
(b) detecting binding of said MOLL polypeptide to said test compound.

30 25. A method for preventing or treating atherosclerosis or a dyslipidemia disorder in humans, said method comprising administering to a human in need thereof an amount of a pharmaceutical composition comprising an agonist or an antagonist of a MOLL polypeptide.

26. A method for preventing or treating atherosclerosis in humans, said method comprising administering to a human in need thereof an amount of a pharmaceutical composition comprising an clk-1 antagonist.

5 27. The method of claim 23 wherein said MOLL nucleic acid is dsc-3 or dsc-4.

28. The method of claim 24 or 25 wherein said MOLL polypeptide is DSC-3 or DSC-4.

10 29. The method of claim 1, 2, 3, or 6, wherein said lipid is cholesterol.

30. The method of claim 1, 2, 3, or 6, wherein said lipoprotein is LDL-like lipoprotein.

15 31. The method of claim 1, 2, 3, or 6, wherein a modified phenotype is detected by (i) visual inspection of the phenotype; (ii) the expression profile of one or more indicator genes; (iii) the expression of one or more reporter genes; (iv) a change in the level and/or distribution of a lipid or lipoprotein in the test nematodes.